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TITLE: Development of Prior Image-Based, High-Quality, Low-Dose Kilovoltage Cone Beam CT for Use in Adaptive Radiotherapy of Prostate Cancer

PRINCIPAL INVESTIGATOR: Xiao Han

CONTRACTING ORGANIZATION: The University of Chicago

Chicago, IL 60637

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INTRODUCTION

Prostate cancer is the most common non-skin cancer and the second leading cause of cancer death among American men [1]. Modern radiotherapy of prostate cancer relies heavily on imaging technologies for accurate patient setup and target localization [2]. In adaptive RT[3], one of the most advanced RT techniques, the treatment plan is adaptively adjusted according to the tumor's change in position, size, and shape [4-6]. Therefore, high-quality 3D images with good soft-tissue contrast are necessary for achieving successful adaptive RT. Kilovoltage CBCT has shown its capability of yielding such images to guide the prostate cancer treatment [7-8]. However, frequent use of high quality CBCT images is often associated with a substantial amount of imaging radiation dose [9-12], which raises concerns about patient safety. On the other hand, one unique feature of clinical CBCT is the availability of a high-quality diagnostic CT image, which can be incorporated in the CBCT image reconstruction as prior knowledge. The objective of this project is to investigate and develop advanced CBCT imaging techniques that utilize prior images for optimized image quality and reduced imaging dose. In the past year, my effort in the proposed project have been supported by a Predoctoral Trainee Award, and I have carried out research tasks as planned. As discussed below, I have implemented narrow beam collimation for CBCT ROI imaging by designing and making necessary hardware devices. I have also created software utilities for synthesizing projection data from prior image and CBCT ROI data, and for performing reconstruction using a standard analytic algorithm. In addition, I implemented imaging geometries different from the conventional circular trajectory for better object coverage. I performed numerical simulation studies and also acquired real data, for which I developed pre-processing methods for data conditioning. I studied the effect of different dose-allocation schemes on the reconstruction image quality, and investigated the effect of key parameters on the performance of image reconstruction by use of iterative algorithms. Throughout the project, I have also carefully designed and computed quantitative metrics to evaluate the image quality, which were used to guide the development and selection of new configurations, algorithms, and parameters. The research that I carried out during the first year was as planned in the proposal, and the the results built a solid basis for continuing further investigation planned for the next year.

1 Research Accomplishments

1.1 Implement narrow beam collimation for CBCT ROI imaging

I have designed and implemented a collimation device and integrated it to the clinical CBCT system. With the add-on device, the current system can perform ROI imaging by acquiring projection data only corresponding to the ROI. I chose to design this device to have similar shape and form factor to the current collimator used to hold the bow-tie filter for X-ray intensity profile shaping, such that additional mechanical complexity is minimized. Another advantage of this design is that mounting is straight forward, which eliminates concerns about mis-alignment with the current system geometry. I then purchased the material, cut it to fit in the enclosure, and fixed it. I then mounted the device to replace the bow-tie filter holder for achieving narrow X-ray collimation. When I finish data acquisition, the bow-tie filter can be put back for normal clinical use.

I acquired numerous narrow beam collimation cone-beam data sets under different configurations using the developed device. First, the two blocking materials were adjusted to have different separation distances for achieving varying degrees of beam collimation, which lead to different sizes of illuminated ROI. Second, I changed different materials for X-ray blocking to reduce the X-ray leakage from the blocked region. Third, I am in the process of developing an improved version of the device with dynamic collimation capability, which can be used to dynamically adjust the degree of collimation during gantry rotation/data acquisition.

1.2 Reproduce the same imaging geometric configurations on CBCT ROI scan as those on prior diagnostic CT scan

Design of numerical and physical phantoms: I first carried out phantom design by using computer-simulation data, which we can select the shape, size, and materials of the structures embedded in a tissue-equivalent environment. I then generated raw projection data using the geometric configuration of the actual CBCT system, including the source-to-isocenter and detectorto-isocenter distances, as well as the angular information for each projection view recorded by the scanner. Furthermore, I considered major physical factors involved in CBCT imaging that deviate data from ideal line-integral projections, which include scatter, beam-hardening, and noise. On top of the raw projection data I simulated scattered X-rays using different scatter-to-primary ratio (SPR) parameters, including the simplified case of a constant profile and more complicated but also more accurate case of convolving the primary photons with a Gaussian kernel. I also obtained the actual X-ray spectrum data measured from the CBCT system under study, which I incorporated in the computer-simulation program for realistic simulation of beam-hardening effect due to the polychromatic nature of the X-ray from the linear accelerator. Furthermore, I added noise to data using a number of different noise models, including Gaussian-, Poisson-, and compound Poisson-distributed noise. I also varied the noise level to mimic different mAs used in clinical and research modes of the CBCT system.

Based upon experiences with the numerical phantom, I designed and made a physical phantom for data acquisition which have insert structures that mimic the density of human organs. I first decided to make the phantom to have similar size to a human head to avoid truncation issues as a starting point, and plan to design and make another larger phantom to have similar size to pelvis. I then looked up the X-ray attenuation coefficients of different plastic materials that have

similar attenuation coefficients to the postate, surrounding soft-tissues, as well as bones. I then obtained the materials from a vendor and assembled the phantom in a plastic enclosure to be filled with water as the background.

Prior diagnostic CT scan and geometry reproduction on CBCT ROI scan: I acquired prior images of the standard calibration phantom and the physical phantom I made using a Philips 64-slice diagnostic CT scanner that I have access to in the Radiation Oncology department. I selected different scanning protocols to acquire data sets of different quality, i.e., noise levels, etc. Though I tried different methods to reproduce the geometric configurations of the prior diagnostic scan on CBCT system, this task proved challenging, mainly for two reasons: (1) the source-to-isocenter and detector-to-isocenter distances are different for the diagnostic scanner and the CBCT scanner and those are difficult, if not impossible, to adjust. (2) the angular position of each projection view are not exactly the same, and interpolation across different views can introduce noticeable loss of spatial resolution.

1.3 Generate data from the prior image based upon the CBCT ROI scan configurations and obtain synthesized projection data

I decided to choose the approach of generating data from the prior image to supplement the missing portion in the CBCT ROI scan. I first reconstructed a prior image from diagnostic scan data using the standard FDK algorithm. I then estimated the size of the CBCT scan ROI in the reconstructed image space, and using this information to remove the corresponding region in the prior image. I then generated data from the prior image with only the peripheral region using a discrete forward projector. The forward projection was carried out according to the exact same geometric configurations used in the CBCT scan, i.e., the same source-to-isocenter and detector-to-isocenter distances as well as identical angular positions. I then combined the forward projected data with the CBCT ROI data to obtain a new, synthesized data set without transverse truncation which is mathematically ready for reconstruction.

1.4 Scatter compensation for synthesized physical phantom data

Compared to diagnostic CT where X-ray beam spanning a relatively small cone-angle is used to illuminate the object, CBCT employs X-ray beam with a much larger cone-angle which illuminates a significantly greater portion of the object/patient [7]. As such, CBCT data contain a much higher component coming from scattered photons rather than primary photons (i.e., photons impinging on the detector after penetrating through the patient along a linear trajectory). This scatter component of the data introduces deviation from and thus inconsistency with the standard X-ray transform model, and therefore must be compensated for or corrected before reconstruction is carried out. The necessity in the particular case of patient prostate localization is critical, as the subtle contrast between the prostate and surrounding soft-tissues can be easily reduced or even diminished by the scatter component having a low spatial frequency. On the other hand, accurate scatter correction is known as a difficult problem because precise knowledge about the physical process of scattering depends on the subject being scanned, and is in general unavailable prior to a CBCT scan. Nonetheless, I developed empirical compensation techniques that can produce an estimate of the scatter profile based upon the physical characteristics of scattered radiation. By appropriately adjusting parameters in the compensation technique, I could minimize the inconsistency between measured data and the assumed imaging model. To verify and demonstrate the

effectiveness of this technique, I compared the reconstructed images before and after performing compensation, which showed that the scatter-induced artifact can be considerably reduced. While proceeding with the scatter-compensated data in following investigation of reconstruction algorithms, I am making continuing effort in optimizing this technique to further improve the accuracy of scatter estimation which can lead to reconstructed images with even better suppressed scatter effect.

1.5 Implement filtered-backprojection reconstruction from the synthesized projection data

I implemented the FDK algorithm, a standard filtered-backprojection type reconstruction algorithm, for carrying out image-reconstruction studies from data acquired and processed in previous steps. I implemented the algorithm in two different programming languages, one in IDL (ITT Visual Information Solutions, Boulder, CO) and another in C. I first wrote the code in IDL for fast debugging and test/validation purpose, and after extensive testing using standard numerical phantoms, such as Shepp-Logan phantom and FORBUILD phantom [8], I implemented the C version for higher execution efficiency. Furthermore, I also implemented in each language an improved version capable of parallel-computation to utilize the multi-core CPU that I have installed on my workstation. The parallel computation of the reconstruction code written in C was implemented by use of OpenMP, and I managed to achieve an approximately 5-fold acceleration on an 8-core CPU compared to the single-thread version. I also modified the IDL code to utilize the built-in multi-threading capability provided by the newest version of the software. On one hand, because three-dimensional image reconstruction is still computationally intensive, I am continuing to improve the efficiency of parallel computation by using more threads. Also I am exploring further improved efficiency of parallel computation enabled by a newly purchased Tesla Graphic Processing Unit (GPU, nVidia, Santa Clara, CA).

I have applied the robust and efficient FDK reconstruction implementation to reconstruct images from data synthesized with prior-image forward projection data and CBCT ROI data. The result shows promising improvement with much reduced truncation artifact. I expect that with better scatter compensation and further improved ROI-to-prior-image registration, image reconstruction of even higher quality can be obtained.

1.6 Investigate and implement different imaging trajectories for CBCT

The current scanning mode of CBCT employs a circular X-ray source trajectory, i.e. the gantry rotates around the subject while the subject itself stays still. Data sampling for this source trajectory inherently limits the reconstructible region, whereas non-conventional source trajectories can potentially expand the reconstructible region. I implemented a reverse-helix trajectory for such purpose. At the time of this phase of investigation, patient couch with programmable translational motion was not available to me. Instead, I made a supporting device capable of translational motion and put it on top of the couch. During data acquisition, I programmed the translation device to feed the object along Z-axis toward the isocenter, while the gantry finishes a full 2π rotation. I then continued to feed the object along the same direction, while rotate the gantry backward for another full turn. This scanning mode accomplishes a reverse-helix source trajectory from the view-point of the object. I implemented a filtered-backprojection (FBP) plus backprojection-filtration (BPF) algorithm [9-11] to reconstruct an image from this reverse-helix data set. Results show that the region that is not reconstructible from circular trajectory data can now be reconstructed. I have

also started to design, implement, and evaluate other source trajectories including a two-circle trajectory and a line-plus-circle trajectory, which may have comparable or further enlarged reconstructible region.

1.7 Investigate optimal CBCT scanning parameters for a given total amount of imaging dose

CBCT image quality can in general improve when the intensity of illuminating X-ray increase, which is also accompanied with higher imaging dose. However, given a total amount of imaging dose, there exists degree of freedoms on how to allocate the total dose to each individual projection view, on the choice of image-reconstruction algorithm, and on the selection of appropriate algorithm parameters, all for the goal of obtaining an image that is optimal in the context of specified imaging tasks. To investigate how these variables impact image quality, I started with studying the effect of dose-allocation parameters, i.e. different combinations of view number and dose per view [11]. For this purpose I fixed the image-reconstruction algorithm as well as the associated parameters, such that the dose-allocation parameters are isolated as the only free variable.

I first carried out a simulation study using the numerical phantom. Keeping the total photon number a constant, I increased the number of views from 30 up to 720, while the number of photons per view decreases proportionally. Then from these data sets I reconstructed images using the FDK algorithm with Hanning window. I designed a set of quantitative metrics to evaluate the effect of different dose-allocation schemes on the reconstruction image quality. I then repeated the experiment using a different total photon number, which itself is a parameter and can have an impact on the results and conclusion. I have collected data and am currently in the process of carrying out data analysis and image-quality evaluation.

I also acquired experimental CBCT data using the calibration phantom, the home-made physical phantom, and anthropomorphic phantom. To minimize data truncation, I designed and made a fixation device to avoid using the patient couch as the support. I then scanned the phantom multiple times with different settings of tube current and exposure time, such that data sets at varying mAs per view are obtained. I then obtain from the full data sets, each consists of 650 views, sparse-view data sets by extracting projection data at a subset of views that are evenly distributed over the scanning range. From these full and sparse-view data sets, I constructed data sets that have the same total mAs (i.e. mAs per view times number of views). In the end, for each of a number of total mAs values, I obtained a number of data sets with different mAs allocation schemes. From each of these data sets, I reconstructed an image using the FDK algorithm with the Hanning window. I am currently in the process of analysing and quantitatively evaluating these images.

1.8 Investigate the appropriate parameter control in total-variation-based image-reconstruction algorithms

Total-variation (TV) based image reconstruction algorithms can potentially yield images from much reduced data (for example, sparse-view data) without significantly compromised image quality [18,19]. Additional knowledge about the object from the prior images can provide potentially remarkable help in reducing the solution space of TV-based algorithms. However, the degree of helpfulness of the prior image also depends on the appropriate selection of algorithm parameters, which have critical impact on the path in the solution-searching process within the

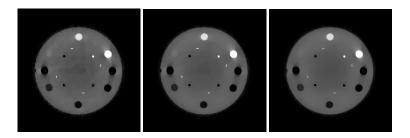


Figure 1: Images of the CATPHAN phantom within the middle transverse slice reconstructed with $\epsilon = 8.6$ (left), 8.65 (middle), and 8.7 (right).

feasible set [20]. I investigated two such parameters, the image array size (or equivalently, the image pixel size), and the data-error tolerance parameter.

Choice of image array size: In TV-based image reconstruction problem the X-ray projection process is modeled as a linear system, and the dimension of the data vector is determined by the physically available elements on the detector. However, the dimension of the image vector remains a free parameter, and a different image array size mathematically defines a different linear system. Choosing a larger image array size may improve spatial resolution due to smaller pixel size, whereas the number of unknowns also increases and enlarges the feasible set, which elevates the underdeterminedness of the linear system and may potentially require more projection views to avoid degradation of image quality. I have studied image reconstruction from numerical phantom and physical phantom data by using a range of pixel sizes, from those below the sampling limit (i.e. the Nyquist spatial frequency in the context of analytic reconstruction) up to four times of the limit. I found that the TV-based algorithm is capable of yielding images of satisfactory quality at over-sampled image grid, and with noise texture closer to images obtained with analytic algorithms. This result can potentially help developing reconstruction techniques that produce images of texture that observers are used to.

Choice of data-error tolerance parameter: As the main framework of the TV-based algorithms under study, we solve the following constrained minimization problem:

$$\mathbf{f}^* = \operatorname{argmin} ||\mathbf{f}||_{TV} \quad \text{s.t.} \quad |\mathcal{H}\mathbf{f} - \mathbf{g}| \le \epsilon \text{ and } f_j \ge 0,$$
 (1)

where the parameter ϵ determines the relaxed tolerance of inconsistency between the modeled linear system and the measured data. Therefore, with other parameters fixed, each ϵ mathematically specifies a unique optimization problem, and, since both $|\mathcal{H}\mathbf{f}-\mathbf{g}|$ and $||\mathbf{f}||_{TV}$ are convex, a unique solution. I designed strategies to determine the range of this key parameter by carefully evaluating the degree of data inconsistency, and experimentally carried out image reconstructions with a range of ϵ [15]. As an example, we display in Fig. 1 images of the CATPHAN phantom reconstructed from real measurement data acquired at 120 views. With increasing ϵ , the images show a gradual trend of smoother appearance with a more uniform background, at the price of some low-contrast structures becoming less discernable and high-contrast objects becoming less sharp, as a trade-off.

1.9 Evaluation of the reconstructed images

Evaluation of reconstructed image quality is critical because in image-reconstruction studies involving real data, reduction of data/imaging dose or introduction of data truncation generally causes degradation of image quality. Therefore, I computed quantitative metrics to closely monitor image quality change as reduced and/or truncated data are used for reconstruction [21]. I first specify the reference image as the ground truth or gold standard, which gives the upper bound of image quality for the study. I used the designed phantom truth and the full-data FDK reconstruction as the reference image for simulation and real data studies, respectively. I then computed the similarity of images reconstructed from ROI data and from sparse-view data with the reference image as a quantitative measure of image quality degradation. Different data-correction methods, image-reconstruction algorithms, as well as choice of algorithm parameters were then compared in the context of these similarity-based metrics, including root mean squared error (RMSE), Pearson correlation coefficient (PCC), and universal image-quality index (UQI) [22], etc. The result shows that the image quality has a sharp improvement when view number increases up to about 100, and then only incremental enhancement is contributed by additional views.

KEY RESEARCH ACCOMPLISHMENTS

- I have implemented a collimation device and mounted it on the CBCT system for ROI data acquisition.
- I have investigated the feasibility of reproducing the geometrical configuration of diagnostic CT scan on CBCT.
- I have generated data from prior image and synthesized it with the CBCT ROI data.
- I have investigated and developed compensation techniques to reduce scatter effect.
- I have implemented filtered-backprojection algorithm for reconstructing images from synthesized projection data.
- I have investigated and implemented non-conventional imaging trajectories for CBCT.
- I have investigated optimal allocation schemes of a given total dose.
- I have investigated the effect of key parameters in TV-based algorithms.
- I have developed strategies for quantitatively evaluating quality of images reconstructed from real data.

REPORTABLE OUTCOMES

Peer-reviewed Journal Papers

- 1. X. Han, J. Bian, D. R. Eaker, T. L. Kline, E. Y. Sidky, E. L. Ritman, and X. Pan, "Algorithm-enabled low-dose micro-CT imaging," *IEEE Transactions on Medical Imaging*, vol. 30 (3), pp 606-620. (Becomes one of the top five most accessed articles of *IEEE Transactions on Medical Imaging* immediately after its publication (March, 2011))
- 2. J. Bian, J. H. Siewerdsen, X. Han, E. Y. Sidky, J. L. Prince, C. A. Pelizzari, and X. Pan, "Evaluation of sparse-view reconstruction from flat-panel-detector cone-beam CT," *Physics in Medicine and Biology*, vol. 55, pp 6575-6599, 2010. (Featured article of *Physics in Medicine and Biology*, published online on Oct-20, 2010, one of the ten most read articles of the journal a few days after its publication until now (Feb-2011), was selected as part of the journal's highlights collection of 2010, cover story of Medicalphysicsweb Review of winter 2011, one of the ten candidates of Roberts' Prize for best paper in *Physics in Medicine and Biology* and the results will be announced in September, 2011.)
- 3. D. Xia, X. Xiao, J. Bian, **X. Han**, E.Y. Sidky, F. De Carlo, and X. Pan, "Image Reconstruction from sparse data in synchrotron-radiation-based micro-tomography," *Review of Scientific Instruments* vol. 82 (4), 2011.

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- 1. **X. Han**, S. Shi, J. Bian, P. Helm, E. Y. Sidky, and X. Pan, "Feasibility study of low-dose intra-operative cone-beam CT for image-guided surgery," Proc. SPIE, 7961, 79615P, 2011
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- 6. J. Bian, J. Wang, **X. Han**, E. Y. Sidky, J. Ye, L. Shao, and X. Pan, "Reconstruction from sparse data in offset-detector CBCT," Proceedings of the First International Conference on Image Formation in X-ray Computed Tomography, 2010
- 7. D Xia, J. Bian, **X. Han**, E. Y. Sidky, J. Lu, O. Zhou, and X. Pan, "Investigation of image reconstruction in CT with a limited number of stationary sources," Proceedings of the First International Conference on Image Formation in X-ray Computed Tomography, 2010

8. **X. Han**, J. Bian, D. R. Eaker, E. Y. Sidky, E. L. Ritman, and X. Pan, "A preliminary study of few-view image reconstruction of sparse objects in cone-beam micro-CT," Proc. SPIE, 7622-96, 2010

Conference Presentations and Abstracts

- X. Han, E. Pearson, J. Bian, S. Cho, E. Y. Sidky, C. A. Pelizzari, and X. Pan, "Toward High-quality, Low-dose Cone-beam CT for Image-guided Radiation Therapy of Prostate Cancer," Innovative Minds in Prostate Cancer Today (IMPaCT), Orlando, FL, March 2011
- 2. **X. Han**, J. Bian, E. Y. Sidky, and X. Pan, "Feasibility study of low-dose intra-operative conebeam CT for image-guided surgery," SPIE Medical Imaging, Orlando, FL 2011
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CONCLUSIONS

During the first year of the project, I have implemented and developed narrow beam collimation for CBCT ROI imaging technique. I have developed hardware device and created software utilities for projection data synthesis of prior image with CBCT ROI data. I implemented a standard analytic image-reconstruction algorithm. In addition, I implemented non-conventional imaging geometries employing reverse-helix source trajectory. I performed numerical simulation studies and also acquired real data, and I developed pre-processing methods for data conditioning. I investigated the impact of dose-allocation parameters on the reconstruction image quality. I also studied the effect of key parameters of TV-based algorithms on the performance of image reconstruction. I have also carefully designed and computed quantitative metrics to evaluate the image quality.

In summary, I have achieved the goals planned for the first year, which have laid down the foundation for the research in the next year. The aims in the next year include further development of the prior image-based, narrowly collimated CBCT imaging technique, prior image-based, sparse-view CBCT imaging technique, and validation and evaluation of the proposed configurations and algorithms.

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